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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/605,283	09/19/2003	Kapil N. Bhalla	1372.76.PRC	2282

21901 7590 06/03/2009

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EXAMINER	
JAGOE, DONNA A	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
06/03/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/605,283	BHALLA ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19,20,23,24 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19,20,23,24 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 19, 20, 23, 24 and 26 are pending in this application.

Applicants' arguments filed May 16, 2008 have been fully considered and they are deemed to be persuasive regarding previous rejections of record. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

However, upon reconsideration, the following rejections and/or objections are newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 20 recites the limitation "the tyrosine kinase inhibitor is imatinib mesylate" in lines 1-2 of the claim. There is insufficient antecedent basis for this limitation in the claim because there is not a tyrosine kinase inhibitor recited in instant claim 19, from which claim 20 depends.

Claim 23 recites the limitation "tyrosine kinase inhibitor" and "histone deacetylase inhibitor" in line 2 of the claim. There is insufficient antecedent basis for this limitation in

the claim because there is no "tyrosine kinase inhibitor" and "histone deacetylase inhibitor" recited in instant claim 19 from which claim 23 depends.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 19, 20, 23, 24 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garattini et al. (Current Opinion in Pharmacology, 2001) and Bernardi et al.(Oncogene 2002)

Garattini et al. teach suberoylanilide hydroxamic acid (SAHA), a histone deacetylase inhibitor (HDAC inhibitor), in the treatment of leukemia (page 360, column 2). It teaches that often, cancer and leukemic cells show altered HDAC activity and several leukemogenic factors cause aberrant recruitment of HDACs. HDAC inhibitors are endowed with cytodifferentiating, antiproliferative and **apoptogenic properties**. Further, Garattini et al. teach that STI571 (imatinib mesylate), a powerful c-Abl inhibitor is in clinical trials for the treatment of **chronic myelogenous leukemia** (page 359, column 2 to page 360, column 1).

Bernardi et al. teach that combinations of complementary or synergistic antitumoural drugs are often utilized in cancer therapy (page 3454 column 2). Further acute promyelocytic leukemia (APL) in mice are treated with SAHA (page 3454, column 2). Further, Bernardi et al. teach that STI517 (Glivec or imatinib mesylate), a potent tyrosine kinase inhibitor inhibits ABL and reduces proliferation of cells in chronic myelogenous leukemia (CML) patients. It was found that with continuous administration of STI517, CML-like tumors could be eradicated (page 3455, column 2).

Both Garattini et al. and Bernardi et al. teach that SAHA and imatinib mesylate are employed for the treatment of leukemias. Neither Garattini et al. or Bernardi et al. teach administration of the agents together.

Addressing the limitation of claim 19, drawn to contacting the living cells with the combination, simple administration of the agents would obviate claims drawn to contacting living cells.

Addressing the limitations of claim 19 wherein the combination is administered when the cancer cells are refractory to imatinib mesylate, in the course of cancer chemotherapy, frequently when agents are used alone the patient becomes refractory. See Bernardi et al. (page 3455, column 2) wherein it is recited that B-ALL is a disease wherein STI 517 is only of temporary benefit. Further, Bernardi et al. teach that combinations of complementary or synergistic antitumoural drugs are often utilized in cancer therapy (page 3454 column 2), providing motivation to employ the two agents imatinib mesylate and suberoylanilide hydroxamic acid for the induce apoptosis in cancer cells, such as chronic myelogenous leukemia, particularly when the cells become refractory to one agent alone.

Addressing the limitation of claim 23, drawn to cell exposure for about 48 hours, Garattini et al. teach that the combination of agents lead to elevated plasma levels following chronic administration (page 359). Although not specifically recited, chronic administration would include infusion of the agents over an extended period, which overlaps with "cell exposure for about 48 hours". Addressing instant claim 26, drawn to cell types of chronic myelogenous leukemia such as accelerated-phase CML cells and blast crisis phase myelogenous leukemia cells, since Garattini et al. teach that STI571 (imatinib mesylate), is in clinical trials for the treatment of **chronic myelogenous leukemia** (CML) (page 359, column 2 to page 360, column 1) and SAHA for treatment

of leukemia (page 360) the recitation of the treatment of CML would obviate claims drawn to specific cell types of CML such as accelerated-phase CML cells and blast crisis phase myelogenous leukemia cells.

One having ordinary skill in the art could have combined SAHA and imatinib mesylate as claimed for the treatment of leukemia and in combination, each element would have performed the same function as it did separately and the results would have been predictable. Further Bernardi et al. teach that combinations of complementary or synergistic antitumoural drugs are often utilized in cancer therapy (page 3454, column 2), providing further motivation to combine the SAHA and imatinib mesylate.
The convenience of putting the histone deacetylase inhibitor (e.g. SAHA) together with the tyrosine kinase inhibitor (e.g. imatinib mesylate) in one composition or method of treatment, though perhaps a matter of great convenience, did not produce a “new” or “different” function and to those skilled in the art, the use of the old elements in combination would have been obvious.

Response to Arguments

Applicant asserts that the recitation of the preamble "imatinib mesylate refractory cancer cells" distinguishes the instant claims from the prior art. In response, See Bernardi et al. (page 3455, column 2) wherein it is recited that B-ALL (strong proliferative blastic leukemia (page 3447)) is a disease wherein STI 517 (imatinib mesylate) is only of temporary benefit. Hence, Bernardi et al. teach that strong proliferative blastic leukemia is eventually refractory to imatinib mesylate. Bernardi et

al. also teach that combinations of complementary or synergistic antitumoural drugs are often utilized in cancer therapy (page 3454 column 2). Further acute promyelocytic leukemia (APL) in mice are treated with SAHA (page 3454, column 2). In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the combination of a histone deacetylase inhibitor to make imatinib mesylate refractory cells more susceptible to the effects of imatinib mesylate) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Applicant asserts that Garattini et al. teaches away from inducing apoptosis but instead teaches the use of compounds for inducing cytodifferentiation in cancer cells. In response, Garattini et al. teach that HDAC inhibitors (e.g. SAHA) are endowed with cytodifferentiating, antiproliferative and **apoptogenic properties.**

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Friday from 8:00 A.M. - 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Donna Jagoe /D. J./
Examiner
Art Unit 1614

June 2, 2009

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614